

### **Remarks**

The final Office action mailed April 20, 2006, has been considered and carefully reviewed. Independent claims 1, 16, 53 and 88 have been amended to specify the first and second assays. The specific types of assays now recited in the independent claims were previously recited in dependent claims (e.g., claims 11, 19, 114, 115, 120, 121) and thus the amendments to claims 1, 16, 53 and 88 should be entered since they do not raise new issues. Independent claim 32 has been amended to specify in more particularity the structure of the nucleic acid array. Support for the amendment to claim 32 is found in the specification, for example, at page 6, lines 22-27 and page 36, lines 29-33. The amendment of claim 32 is in response to the examiner's new statement on page 10 of the final Office action that "neither the array nor microarray are defined, described or limited by structure and/or size." Since this explanation first appeared in the final Office action, applicants should be given the opportunity after a final Office action to amend claim 32 to address the concerns of the examiner. Accordingly, entry of the amendment to claim 32 is also respectfully requested.

### **35 U.S.C. §102 Rejections**

Claims 1-2, 4-9, 11-12, 14, 16-20, 29-30, 49, 53-61, 70, 87-89 and 91-92 were rejected under 35 U.S.C. §102(b) over Enghardt et al. Independent claims 1, 16 and 88 have been amended to indicate that at least one of the first or second assay comprises at least one nucleic acid hybridization. Independent claim 53 has been amended to indicate that at least one of the first agent or the second agent comprises a nucleic acid probe. There is no mention in Enghardt et al. of any type of nucleic acid analysis or the use of a nucleic acid probe. Accordingly, the pending 35 U.S.C. §102(b) rejection of claims 1, 16, 53, and 88 (and the dependent claims thereof) must be withdrawn.

Claims 32-42 have been rejected under 35 U.S.C. §102(e) over An et al. Claim 32 has been amended to specify that the nucleic acid array comprises at least hundreds of different nucleic acid sequences affixed to the surface of a support and arrayed in assigned locations in the shape of a grid. As discussed in the January 30, 2006, Amendment and Reply, An et al. discloses plating a cDNA

library on agarose plates. Subsequently, “[i]ndividual colonies are transferred to nylon or nitro-cellulose membranes and the EST probes are hybridized to complementary sequences on the membranes” (column 3, lines 39-41) (emphasis added). The cDNA library plated on the agarose plates is not itself used in the An et al. process for screening multiple genes in a biological specimen as required by the nucleic acid array in claim 32. Accordingly, the cDNA library plated on the agarose plates cannot be a nucleic acid array as recited in claim 32. With respect to the cDNA colonies residing on the nylon or nitro-cellulose membranes in the An et al. process, there is nothing in An et al. disclosing that such colonies are “arrayed in assigned locations in the shape of a grid” or that there are “at least hundreds of different” colonies affixed to the surface of a support. Since An et al. fails to teach these features of claim 32, the pending 35 U.S.C. §102(e) rejection of claim 32-42 over An et al. must be reconsidered and withdrawn.

### 35 U.S.C. §103 Rejections

Dependent claims 22, 46-48 and 98-100 have been rejected for obviousness in view of Enghardt et al. However, as explained above, the teaching in Enghardt et al. is fatally deficient with respect to the base independent claims. Thus, an obviousness rejection over Enghardt et al. alone also must be fatally flawed.

Dependent claims 24-28 and 114-123 have been rejected for obviousness in view of Enghardt et al. combined with An et al. With respect to claims 114, 115, and 119-123 the Office action on page 12 states that “An et al. teach the similar method wherein further examination of tissues at the antibody and/or nucleic acid level is used to further distinguish tumor from non-tumor samples (Column 58, line 55-column 59, line 7).” A close inspection of the above-cited passage in An et al. reveals that there is no disclosure or suggestion of employing both an immunological analysis and a nucleic acid hybridization as now recited in independent claims 1, 16 and 88. An et al. simply makes the speculative statement at column 59, lines 5-7, that “[e]xamination of tissue by in situ hybridization *or* by immunohistochemical methods *may* be required to distinguish between these possibilities.” (emphasis added). First, this statement refers to “in situ hybridization *or* by immunohistochemical methods” rather than in situ hybridization *and* immunohistochemical methods. In contrast, the

methods of claim 1, 16 and 88 contemplate the combination of both an immunological analysis and a nucleic acid hybridization. Second, this statement is simply a speculative suggestion to possibly try examining the tissue in question with in situ hybridization *or* immunohistochemical methods. There does not appear to be any examples in An et al. that employed the presently recited combination. Thus, a person of ordinary skill in the art reading An et al. would not have been motivated to utilize an immunological analysis and a nucleic acid hybridization.

Dependent claims 31, 50-52, 62-63, 68-69, 71-78 and 86 have been rejected for obviousness over Enghardt et al. combined with Stapleton et al. Stapleton et al. is relied upon for allegedly disclosing the analysis of certain specific types of tissue. However, there is nothing in Stapleton et al. that cures the above-discussed deficiencies in Enghardt et al. Thus, the pending obviousness rejection of Enghardt et al. combined with Stapleton et al. must be withdrawn.

Dependent claims 66 and 67 have rejected for obviousness over Enghardt et al. combined with Stapleton et al. and An et al. However, as explained above, neither Stapleton et al. nor An et al. cures the fatal deficiencies in Enghardt et al. with respect to the base independent claims.

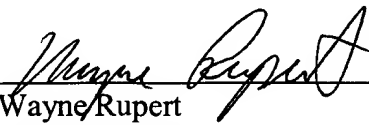
It is respectfully submitted that the present application is in condition for allowance. Should there be any questions regarding this application, examiner Forman is invited to contact the undersigned attorney at the telephone number shown below.

Respectfully submitted,

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